

INTERNATIONAL SEARCH REPORT

International application No.

PCT/ ES 2005/070017

A. CLASSIFICATION OF SUBJECT MATTER

IPC⁷ A61K 31/185, , A61P 35/00, A61P 17/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC⁷ A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CIBEPAT, EPODOC, REGISTRY, HCAPLUS, EMBASE, BIOSIS, MEDLINE.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NOUR A.F. & SALAM S. Preliminary clinical study with calcium dobesilate in fibrocystic disease of the breast, a pilot study. Invasive Treatment. 1986, Volume 12, Nº 3, pages 233-242. The whole document.	1,2,5-7
X	RUIZ, E. & TEJERINA, T. Calcium dobesilate increases endothelium-dependent relaxation in endothelium-injured rabbit aorta. Pharmacological Research. 1998, Volume 38, Nº 5, pages 361-366. (abstract) HCAPLUS [on line] [recovered on 02.02.2005]. Recovered from: STN International, Columbus, Ohio (EE.UU.). Access Nr. 1999:6013.	1,6
A	GRABER, R. y col. Calcium dobesilate protects human peripheral blood mononuclear cells from oxidation and apoptosis. Apoptosis. 1998, Volume 3, Nº 1, pages 41-49. (abstract) HCAPLUS [on line] [recovered on 02.02.2005]. Recovered from: STN International, Columbus, Ohio (EE.UU.). Access Nr. 1998:171183.	1,2,6

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

13 June 2005 (13.06.05)

Date of mailing of the international search report

22 June 2005 (22. 06.05)

Name and mailing address of the ISA/

SPTO

Authorized officer

Facsimile No.

Telephone No.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

(PCT Rule 43bis.1)

		Date of mailing (day/month/year) 22 JUN 2005
Applicant's or agent's file reference PCT183		FOR FURTHER ACTION See paragraph 2 below
International application No. PCT/ES2005/070017	International filing date (day/month/year) 16.02.2005	Priority date (day/month/year) 17.02.2004
International Patent Classification (IPC) or both national classification and IPC A6K31/185, A61P 35/00, A61P 17/06		
Applicant INVESTREAD EUROPA, S.L.		

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

**CORRECTED
VERSION**

Name and mailing address of the ISA/ES	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/ES2005/070017

Box No. I	Basis of this opinion
<p>1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.</p> <p><input type="checkbox"/> This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).</p> <p>2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:</p> <p>a. type of material</p> <p><input type="checkbox"/> a sequence listing</p> <p><input type="checkbox"/> table(s) related to the sequence listing</p> <p>b. format of material</p> <p><input type="checkbox"/> in written format</p> <p><input type="checkbox"/> in computer readable form</p> <p>c. time of filing/furnishing</p> <p><input type="checkbox"/> contained in the international application as filed.</p> <p><input type="checkbox"/> filed together with the international application in computer readable form.</p> <p><input type="checkbox"/> furnished subsequently to this Authority for the purposes of search.</p> <p>3. <input type="checkbox"/> In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.</p> <p>4. Additional comments:</p>	

**WRITTEN OPINION OF THE
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International application No.
PCT/ES2005/070017

Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement																												
<p>1. Statement</p> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 25%;">Novelty (N)</td> <td style="width: 50%;">Claims</td> <td style="width: 25%; text-align: right;">YES</td> </tr> <tr> <td></td> <td><u>3-4, 8-14</u></td> <td></td> </tr> <tr> <td></td> <td><u>1, 2, 5-7</u></td> <td style="text-align: right;">NO</td> </tr> <tr> <td style="padding-top: 10px;">Inventive step (IS)</td> <td>Claims</td> <td style="text-align: right;">YES</td> </tr> <tr> <td></td> <td><u>3-4, 8-14</u></td> <td></td> </tr> <tr> <td></td> <td><u>1, 2, 5-7</u></td> <td style="text-align: right;">NO</td> </tr> <tr> <td style="padding-top: 10px;">Industrial applicability (IA)</td> <td>Claims</td> <td style="text-align: right;">YES</td> </tr> <tr> <td></td> <td><u>1-14</u></td> <td></td> </tr> <tr> <td></td> <td>Claims</td> <td style="text-align: right;">NO</td> </tr> </table>			Novelty (N)	Claims	YES		<u>3-4, 8-14</u>			<u>1, 2, 5-7</u>	NO	Inventive step (IS)	Claims	YES		<u>3-4, 8-14</u>			<u>1, 2, 5-7</u>	NO	Industrial applicability (IA)	Claims	YES		<u>1-14</u>			Claims	NO
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<p>2. Citations and explanations:</p> <p>Documents taken into consideration:</p> <table border="1" style="width: 100%; border-collapse: collapse; text-align: center;"> <thead> <tr> <th style="width: 15%;">Doc.</th> <th style="width: 60%;">Publication or identification no.</th> <th style="width: 25%;">Publication date</th> </tr> </thead> <tbody> <tr> <td>D1</td> <td>Acta Therapeutica, vol. 12, no. 3</td> <td>1986</td> </tr> <tr> <td>D2</td> <td>Pharmacological Research, vol. 38, no. 5</td> <td>1998</td> </tr> </tbody> </table>			Doc.	Publication or identification no.	Publication date	D1	Acta Therapeutica, vol. 12, no. 3	1986	D2	Pharmacological Research, vol. 38, no. 5	1998																		
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D1	Acta Therapeutica, vol. 12, no. 3	1986																											
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<p>The invention relates to the use of 2,5-dihydroxybenzenesulphonic acid (dobesilate), in particular its calcium and potassium salts, in the treatment of angiodependent diseases and diseases involving a reduction in apoptosis such as cancer and psoriasis.</p>																													
<p>Document D1 describes the use of calcium dobesilate in the treatment of fibrocystic breast disease, a benign tumour that appears in the last decade of a woman's reproductive life as a result of a hormonal imbalance.</p>																													
<p>Document D2 relates to the use of calcium dobesilate as an angioprotector (particular case of angiodependent diseases) in some vascular diseases such as diabetes associated with retinopathies.</p>																													

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Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	
<p>Claims 1, 2, 5-7 of the application are therefore not considered to be novel based on the disclosures of the above documents (PCT Article 33(2)).</p> <p>However, as pointed out in the examples of the application, dobesilate exhibits antiproliferative, antiangiogenic, antimigratory and proapoptotic properties of these compounds in tumour cells (non-quiescent) and in chronic psoriasis plaques.</p> <p>None of the documents mentioned above has been found to contain any reference or information that could lead a person skilled in the art to apply the compound to the treatment of cancer or psoriasis.</p> <p>Claims 3-4 and 8-14 of the application are therefore considered to comply with the requirements of novelty, inventive step and industrial applicability (PCT Article 33(2), (3) and (4)).</p>		